In the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Listings of claims

1. (Original) A carboxypeptidase U (CPU) mutant polypeptide having greater thermal stability than the wild-type polypeptides, which mutant possesses at least two amino acid substitutions relative to the wild-type polypeptide, at least one of which is located at an amino acid residue position relative to SEQ ID NO: 2 selected from: 327, 355 and 357.

2. (Original) A carboxypeptidase U (CPU) mutant polypeptide according to claim 1, wherein at least two of the amino acid substitutions are selected from: 327, 355 and 357.

3. (Original) A CPU mutant polypeptide as claimed in claim 1, wherein there are at least 3 substitutions.

4. (Original) A CPU mutant polypeptide according to claim 1, which is a human polypeptide.

5. (Original) A CPU mutant polypeptide according to claim 1, which is a mouse or rat polypeptide.

6. (Original) A CPU mutant polypeptide according to claim 4, wherein at least one of the substitutions is selected from the group consisting of: S327C, H355Y, H357P and H357Q.

7. (Original) A CPU mutant polypeptide according to claim 6, wherein at least one of the substitutions is selected from the group consisting of: K166N, I204T, V219A, Y230C, I251T, H315R, S327C, K346N, S348N, K349R, N350S, R352K, H355Y, H357P and H357Q.

8. (Original) A CPU mutant polypeptide according to claim 1, which mutant possesses an amino acid substitution at each of positions: S327, H355 and H357, relative to SEQ ID NO:2.

9. (Original) A CPU mutant polypeptide according to claim 1 or claim 2, comprising the sequence selected from: SEQ ID NO: 17, 18 and 19.

10. (Original) A nucleic acid molecule encoding a polypeptide according to claim 1~~any of claims 1-9~~.

11. (Currently Amended) A nucleic acid molecule encoding a polypeptide according to claim 1~~any of claims 1-9~~ and a CPU prepro sequence.

12. (Original) A vector comprising a nucleic acid according to claims 10 or 11.

13. (Original) A cell comprising the nucleic acid according to claims 10 or 11.

14. (Currently Amended) A method of producing a CPU mutant polypeptide according to claim 1 ~~any of claims 1-9~~, comprising cultivating a cell according to claim 13, under conditions suitable to allow expression of the polypeptide and isolating the CPU mutant polypeptide produced.

15. (Currently Amended) A purified antibody, capable of selectively binding to a CPU mutant polypeptide according to claim 1 ~~any of claims 1-9~~.

16. (Currently Amended) A pharmaceutical composition comprising a therapeutically effective amount of the mutant CPU according to claim 1~~any of claims 1-9~~, and a pharmaceutically effective excipient or diluent.

17. (Currently Amended) A method of treating, preventing, managing or ameliorating the symptoms of hemorrhagic disease or disorder comprising administration of a therapeutically effective amount of a pharmaceutical composition according to claim 16.

18. (Currently Amended) A method of causing blood to clot comprising contacting the blood with an effective amount of a CPU mutant comprising the amino acid sequence according to SEQ ID NO: 2, but with at least two amino acid substitutions, at least one of which is at a position selected from the group consisting of: 327, 355 and 357.

19. (Currently Amended) A method of producing a crystal structure of a CPU mutant polypeptide according to claim 1~~any one of claims 1 to 9~~, comprising allowing the polypeptide produced according to claim 14 to form a complex with a Fab fragment, purifying the complex and treating the purified complex under conditions suitable to allow crystal formation.

20. (Currently Amended) The method of producing wild-type CPU or proCPU crystals, comprising mixing together purified CPU or proCPU polypeptide with a Fab fragment

directed to all or part of amino acids from positions 327 to 357 inclusive (according to the position in SEQ ID NO: 2) so as to allow complex formation, purifying the complex and treating the purified complex under conditions suitable to allow crystal formation.

21. (Currently Amended) A crystal of a mutant CPU polypeptide according to claim 1~~any one of claims 1 to 9~~.